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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,365	07/07/2003	Christopher J. M. Meade	1/1364	7867

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EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,365	MEADE ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7-11,13,19-38,43 and 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-11,13,19-38,43 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted October 27, 2006 wherein claims 1, 7-11, 19, 23-25, 28-30, 37, and 38 are amended, claims 3, 6, 12, 14-18, and 39-42 are cancelled, and new claim 44 is introduced . This application claims benefit of provisional application 60/407895, filed September 3, 2002 and foreign application DE10230769.5, filed July 9, 2002.

Claims 1, 2, 4, 5, 7-11, 13, 19-38, 43, and 44 are pending in this application.

Claims 1, 2, 4, 5, 7-11, 13, 19-38, 43, and 44 as amended are examined on the merits herein.

Applicant's amendment, filed October 27, 2006, with respect to the rejection of claim 6 under 35 USC 112, second paragraph, for indefiniteness for reciting improper chemical names and the trademark Ariflo®, has been fully considered and found to be persuasive to remove the rejection as claim 6 is no longer pending. Thus the rejection is withdrawn.

Applicant's amendment, filed October 27, 2006, with respect to the rejection of claims 1-5 and 8-43 under 35 USC 112, first paragraph, for lacking enablement for any unspecified PDE4 inhibitors, has been fully considered and found to be persuasive to remove the rejection as the claims are now drawn to a well-defined group of DPE4 inhibitors which are adequately enabled by Applicant's disclosure. Thus the rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4, 5, 7-11, 13, 19-38, 43, and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims recite a number of chemical names, including Bay-198004, CP-325366, BY343, D-4396, V-11294A, and AWD-12-281. These names are not standard chemical or trivial names and do not clearly and definitely identify which compounds are indicated, thereby rendering the claims indefinite.

Response to Argument: Applicant's amendment and remarks with attachment A, filed October 27, 2006, with respect to the rejection of previous claims 6 and 7 on similar grounds, has been fully considered and not found persuasive to remove the rejection. Applicant argues that the recited names are in fact widely accepted chemical names for the claimed substances. However, the recited names are not suitable as a unique, definite trivial name for the purpose of patent prosecution. This name bears an extremely close resemblance to the temporary designations given to lead compounds in a combinatorial library, for example. For this reason, it is very likely that, either currently or in the future, there exist, or will exist, by pure chance, other chemical compounds designated as Bay-198004, or D-4396, for example. A trivial name only satisfies the requirements of 35 USC 112, second paragraph if there is a reasonable expectation of

the name actually being unique both now and in the future. For example, the names, "(III)," "Compound X," "Sodium salt 4," or "lipophilic amine," would not be acceptable designations under 35 USC 112, second paragraph, even if they had obtained a measure of recognition as common names for a particular compound.

Thus Applicants arguments are not found convincing to remove the rejection. Because Applicant's amendment necessitated this new ground of rejection, this rejection is made **FINAL**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 5, 7-11, 13, 19-38, 43, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knowles et al. (PCT international publication WO03/011274, reference included with PTO-1449) in view of Meissner et al. (US patent 6706726, cited in PTO-1449) further in view of Hill et al. (US patent 6060069, reference cited in PTO-892) Knowles et al. discloses combinations of an anticholinergic and a PDE-4 inhibitor and methods for their use in preventing or reducing the symptoms of pulmonary disease. (p. 1, lines 1-7) Theophylline is mentioned as an example of a PDE-4 inhibitor, although any PDE-4 inhibitor may be included within the scope of the invention. (p. 3, lines 25-26) An example is provided of a pharmaceutical dose

formulation which comprises a 1:1 ratio of cliomilast and tiotropium bromide, an anticholinergic, in 18 μg each in a metered dose inhaler with 1,1,1,2-tetrafluoroethane, also known as TG134a, (p. 10, table 1, lines 4-9) falling within the limitations of instant claims 8-13 and 19-22 for use in an inhaler according to instant claim 40. Another embodiment is a powder formulation for a dry powder inhaler comprising cliomilast and tiotropium bromide mixed with lactose as an excipient, (p. 10, lines 10-19) in the limitations of instant claims 11-14, enclosed in a hard gelatin capsule and enclosed in an inhaler according to instant clams 14, 17 and 40. The formulation for nasal administration described on p. 10, lines 20-29 contains hydrochloric acid, a pharmaceutically acceptable inorganic acid according to instant claim 44. Knowles et al. does not disclose a pharmaceutical combination comprising **1** and a PDE-4 inhibitor. Knowles et al. also does not disclose an inhalable powder having a particle size of up to 250μm or between 10 and 150μm, as described in instant claims 15-16 or an inhalable powder comprising only **1** and **2** as described in instant claim 18, or a propellant containing inhalable aerosol containing additional ingredients according to instant claim 23, or a propellant-free inhalable solution according to instant claims 25-38.

Meissner et al. discloses anticholinergic compounds of a general formula which includes **1** as an embodiment. (Example 1, column 10, lines 10-29) These agents are expected to be useful in the treatment of chronic obstructive pulmonary disease and asthma. (column 19, lines 63-65) Meissner et al. specifically discloses that these compounds may be administered by inhalation. (column 22, lines 26-29) Specific formulations described by Meissner et al. include an aerosol spray for use in an inhaler,

(column 24, lines 40-55) an inhalable solution according to instant claims 25-29, 32, 33, 36, and 39 for use in an inhaler according to instant claim 42, (column 24, lines 58-67) and a powder comprising the active substance and lactose monohydrate. (column 25, lines 15-20)

Hill et al. discloses a method of treating pulmonary disease by administering a drug as an inhalable powder using lactose as an excipient, in which the lactose particles are in the size range of between 20 and 100 microns. (column 3, lines 38-46)

It would have been obvious to one of ordinary skill in the art at the time of the invention to produce a composition similar to those disclosed by Knowles et al. comprising the anticholinergic drug of Meissner et al. in place of the anticholinergics disclosed by Knowles et al and to use this combination in the therapeutic method of claim 43. It would also have been obvious to one of ordinary skill in the art to prepare this composition as an inhalable powder comprising the active ingredients and lactose with a particle size of between 20 and 100 microns as described by Hill et al, or an inhalable powder comprising only **1** and **2**. It would furthermore have also been obvious to prepare the pharmaceutical composition as a propellant-containing aerosol containing additional ingredients as described in claim 23, or as a solvent-free inhalable aerosol as described in claims 25-39.

One of ordinary skill in the art would have been motivated to prepare the composition using the anticholinergic compound **1** of Meissner et al. in place of the anticholinergics of Knowles et al. because this compound is also an anticholinergic, is structurally similar to the compounds of Knowles et al., and is useful for treating the

same condition. (i.e. obstructive pulmonary disease) One of ordinary skill in the art would have been motivated to prepare the composition as an inhalable powder additionally comprising lactose with a particle size of between 20 and 100 microns because a similar composition is disclosed by Hill et al. for the pulmonary delivery of a different drug. One of ordinary skill in the art would have been motivated to prepare an inhalable powder containing only **1** and **2**. because the lactose excipient is an inert carrier which is not essential to the biological function of the active ingredient. One of ordinary skill in the art would have been motivated to prepare a propellant-containing aerosol containing additional ingredients as described by claim 23 because adding standard ingredients such as preservatives, stabilizers, and surfractants is standard practice in the art. One of ordinary skill in the art would have been motivated to prepare the composition as a propellant-free aerosol according to claims 25-29, 32, 33, and 36 because Meissner et al. discloses such a solution as a means for pulmonary delivery of the anticholinergic. One of ordinary skill in the art would have been motivated to add to this solution a co-solvent according to claims 30-31 and to add an antioxidant because determining the exact solvent composition and excipients of a pharmaceutical composition is a routine procedure in the art. One of ordinary skill in the art would have been motivated to use sodium EDTA in this solution because Meissner et al. discloses a solution comprising EDTA and sodium EDTA is a common form of EDTA. One of ordinary skill in the art would have been motivated to prepare the solution with only benzalkonium chloride or benzalkonium chloride and sodium EDTA because these solutions consist essentially of the same ingredients as the propellant-free solution

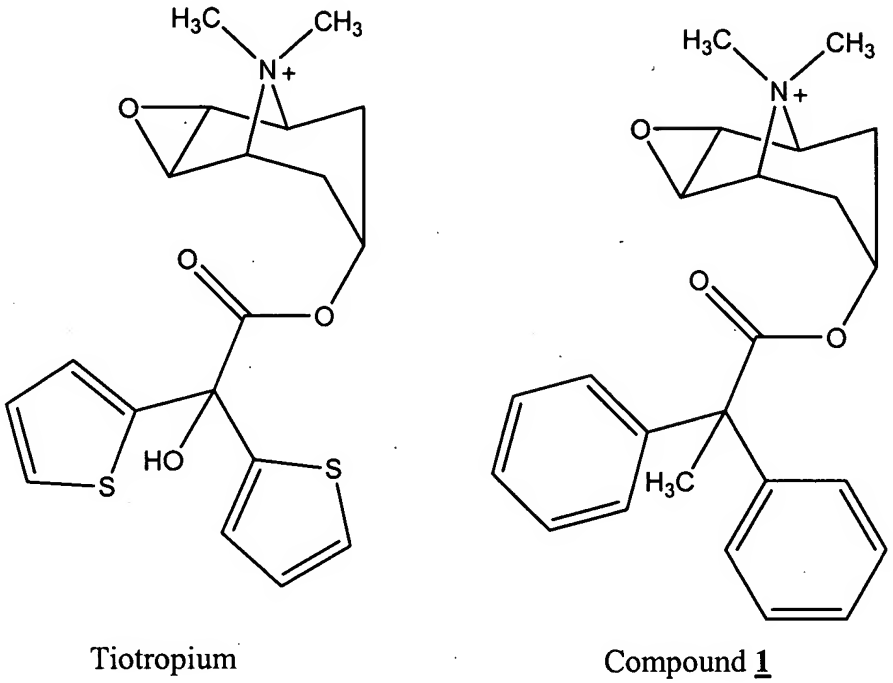
disclosed by Meissner et al. and differ only in the absence of HCl, which is not essential to the biological function of the active ingredient.

One of ordinary skill in the art would have reasonably expected success in preparing the pharmaceutical composition with the compound of Meissner et al. because of the similarities between this compound and those already known to be useful in this invention. One of ordinary skill in the art would reasonably have expected success in preparing an inhalable powder with a particle diameter between 20 and 100 microns and an inhalable solution according to claims 25-29, 32, 33, and 36 because these formulations are taught in Meissner et al. and Hill et al. to be useful for pulmonary delivery of drugs. One of ordinary skill in the art would have been motivated to make various minor modifications such as adding ingredients as described by claims 23, 30, 31, 34, and 35 or subtracting them as described in instant claims 18, 36, and 37 because these modifications are minor modifications which are well within the routine skill of one of ordinary skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, filed October 27, 2006, with respect to the above rejection, have been fully considered and not found persuasive to remove the rejection. Applicant argues that the anticholinergics disclosed by Knowles et al. are sufficiently different in structure and biological activity from those of Meissner et al. to preclude any suggestion of using them in the compositions of Knowles et al. However, the compound **tiotropium bromide**, which is explicitly disclosed by Knowles et al. as an example of an anticholinergic useful in the compositions of Knowles et al., is

structurally similar to compound **1** and the other compounds of Meissner et al., as shown in figure 1 below:



Tiotropium Compound **1**

FIGURE 1

Furthermore, although Meissner discloses that, "the benzilic acid esters of scopine, tropenol, and tropine disclosed in WO92/16528," are not satisfactory for once per day dosing, Meissner et al. does not say the same about tiotropium bromide. Considering that tiotrpoium bromide is closer in structure to compound **1** than it is to atropine, scopolamine, or any of the other compounds of Knowles et al. which Applicant names as being distinct from compound **1**, one of ordinary skill in the art would in fact recognize it as being similar to **1** and would therefore be motivated to combine the teachings of the various references as described above.

Thus the rejection is maintained and made **FINAL.**

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 4, 5, 7, and 43 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of US patent application 10/613783 (Cited in PTO-1449, herein referred to as '783) in view of claims 1-8, 11, and 21-23 of U.S. Patent No. 6706726 (Meissner et al, cited in PTO-1449) Claims 1-10 of '783 et al. are drawn to combinations of an anticholinergic drug with a PDE-IV inhibitor. Claims 5 and 6 of Pairet et al. are drawn to such a composition in which the anticholinergic is a tiotropium, oxitropium, or ipratropium salt. These classes of anticholinergics share a substantial structural similarity with the claimed compound 1. Claims 9-10 of Pairet et al. disclose compositions comprising an

anticholinergic and a PDE-IV inhibitor in which the PDE-IV inhibitor is one of the exact same inhibitors recited in instant claims 6-7. Claim 13 of Pairet et al. discloses a pharmaceutical composition of an anticholinergic drug and a PDE-IV inhibitor which is suitable for inhalation. Claims 1-13 of '783 et al. do not disclose a pharmaceutical combination comprising 1 and a PDE-4 inhibitor.

Claims 1-5 of Meissner et al. are drawn to anticholinergic compounds of a general formula which includes 1 as an embodiment. Claim 11 is drawn to the compound 1 itself. Claims 6-8 and 21-23 are drawn to methods of using this compound in the treatment of conditions including chronic obstructive pulmonary disease and asthma.

It would have been obvious to one of ordinary skill in the art at the time of the invention to produce a composition similar to those disclosed by Pairet et al. comprising the anticholinergic drug of Meissner et al. in place of the anticholinergics disclosed by Pairet et al. and to use this combination in the therapeutic method of claim 43. One of ordinary skill in the art would have been motivated to prepare the composition using the anticholinergic compound 1 of Meissner et al. in combination with a PDE-4 inhibitor as described by Pairet et al. because the compounds in the compositions of Pairet et al. also contain anticholinergics which are structurally similar to compound 1, and are useful for treating the same condition. (i.e. obstructive pulmonary disease) One of ordinary skill in the art would have reasonably expected success in preparing the pharmaceutical composition with the compound of Meissner et al. because of the

similarities between this compound and those already known to be useful in this invention.

This is a provisional double patenting rejection because the conflicting claims have not yet been patented.

Response to Argument: Applicant's arguments, filed September 27, 2006, with respect to the above provisional obviousness-type double patenting rejection, are identical to those discussed above with respect to the rejection of instant claims 1, 2, 4, 5, 7-11, 13, 19-38, 43, and 44 under 35 USC 103, and are not found persuasive to remove the rejection for reasons described above. Thus this rejection is made **FINAL**.

Conclusion

No claims are allowed in this application. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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